REMARKS

Claim 1 has been amended as follows:

1. The first region that is excised and the second region that replaces it each "consist essentially of" the nucleotide sequence encoding an acyltransferase (AT) domain. This clarifies that only the AT-encoding domain and not additional activities in the module are excised and replaced. This amendment is supported, for example, on page 3 at lines 21-24 and by Examples 1 and 2.

2. Claim 1 now requires that both excised AT domain encoding regions are excised by a restriction enzyme reaction and insertion is by ligation. Support for this limitation is found, for instance, on page 12, lines 23-28, page 11, lines 1-2, and by Examples 1 and 2.

3. Claim 1 is amended to require that the modular PKS from which the first extender unit is excised is not the modular PKS from which the second extender unit is obtained. This is supported on page 10, lines 1-2, and by Examples 1 and 2.

Claim 7 has been amended by inserting the limitations of former claims 8 and 9. New claim 31 is dependent on claim 1 and is supported in the specification on page 12 at lines 26-28. Thus, no new matter has been added and entry of the amendment is respectfully requested.

The Rejections Under 35 U.S.C. § 112, First Paragraph / Written Description and Enablement

The basis for these rejections appears to be the same in both cases. Basically, the argument of the Office is that because the nucleotide sequences encoding only two modular PKS-encoding gene clusters had been reported at the time the application was filed, the illustrative examples which involve erythromycin and rapamycin-encoding clusters are insufficient to describe or enable the genus of methods claimed.

Respectfully, the Office appears to be applying the standard for claiming new compositions of matter/new molecules in a generic manner with the standard for claiming generic methods, when there is no reason to believe that the methods as disclosed would be inapplicable to other members of the genus of compositions known to exist.

At the time the application was filed, it was understood that all PKS modular proteins were organized in a similar manner. That is, they all contained modules wherein each module contained three required enzyme activities – KS, AT and ACP, and optionally contained an activity to effect reduction of the resultant carbonyl group. Because of the similarity of organization of the modular PKS sequences, which was known at the time the application was filed, there is no reason to doubt that the further refinement to the generalized scaffolded structure recognized by applicants in the two exemplified PKS would not be characteristic of the remaining members of this extensive family. Basically, applicants recognized that the modules contained domains responsible for the catalytic activities that were separated by sufficient "scaffolding" to permit individual enzymatic activities to be excised and exchanged. While Katz (discussed below) interchanged various regions of the DEBS PKS, there is no report in Katz of isolating an individualized precisely bounded catalytic domain and placing it into a modular PKS from which a similarly precisely defined catalytic region had been excised.

Since applicants are not claiming a new structure, which indeed needs to be defined precisely in structural terms and with respect to sufficient members of a genus to justify claiming of the genus itself, the claimed methods require no such precise description in order to evidence that the applicants had possession of the invention and thus fulfilled the written description requirement or to enable those of skill in the art to practice it on any arbitrary modular PKS gene cluster.

As demonstrated by the DEBS and rapamycin PKS gene clusters described in the application, there is sufficient homology in the catalytic regions to permit such regions to be identified in any newly discovered or sequenced PKS thus permitting the critical insight of the present applicants to be taken advantage of by applying standard recombinant molecular biology techniques.

In summary, applicants believe the criterion quoted by the Office, evidently from *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) is not applicable to the present claims. *Eli Lilly* involved claiming new molecules that needed to be defined structurally in order to be distinguished from other compositions. In that case, it makes sense that a representative number of species would be required in order to claim a genus. Here, however, the generic method described is applicable to all members of the genus that exhibit the characteristic features of modular PKS proteins. It was understood at the time the application was filed that the generic characteristics of modular PKS proteins and their encoding sequences were exhibited in common among them.

For this reason, it is believed that the rejections under 35 U.S.C. § 112, both for written description and enablement, may properly be withdrawn.

The Rejections Under 35 U.S.C. § 102

The pending claims were all rejected as anticipated under § 102(b) by Katz (WO 93/13663) or under 35 U.S.C. § 102(e) as anticipated by Katz (U.S. patent 5,824,513 ('513)).

Both documents contain substantially the same disclosure. There is no dispute regarding that point.

The Office points to claim 1 of the '513 patent which contains a number of steps. Step c), in one alternative, describes substitution of one acyltransferase domain with another "isologous" acyltransferase domain of different specificity.

There are at least three reasons why the method of claim 1 herein is not anticipated.

1. Claim 1 as amended requires that any "substitution" of AT domains be by a region "consisting essentially of" the nucleotide sequence encoding the AT domain. This limitation is not met in the underlined portion of the '513 claim, which simply requires that the AT domain be included in whatever is substituted.

2. The underlined portion of the '513 claim requires an "isologous acyltransferase." This is excluded from the claims as amended which require that the modular PKS from which the first extender unit is excised is not the modular PKS from which the second extender unit is obtained.

3. Perhaps most telling, the claims as amended require that both the first and second AT domain-encoding regions have been excised by restriction enzyme reaction, and that the first region be ligated into the recipient PKS encoding sequence. There is no language in the quoted claim, or any disclosure in the entire cited documents, of using restriction enzymes for both excisions and for ligation into the recipient DNA. The entire process claimed in claim 1 must be conducted using restriction enzymes both for excising the AT-encoding domains and for inserting them back by ligation into a different modular PKS.

Similarly, as to claim 7 and its dependent claims, there is no disclosure of using donor and recipient plasmids with different selectable markers wherein the donor plasmid is temperature sensitive in either of the Katz documents.

Accordingly, the rejection for anticipation over Katz (WO 93/13663) and Katz (US 5,824,513) may properly be withdrawn.

All claims were rejected as anticipated under 35 U.S.C. § 102(e) by US 6,200,813 ('813). Applicants appreciate the acknowledgement of their previous arguments and believe that these were correct. If, indeed, claim 1 of the '813 patent is supported by the disclosure of the '513 specification or claims, then citation of the '513 patent should be sufficient. Respectfully, there is no justification for citing the '813 patent which contains subject matter not present in '513 and which thus has a § 102(e) date later than the effective date herein, as a reference against the present claims.

Again, respectfully, applicants do not follow the argument that since claim 1 of the '513 patent is enabled in its application, claim 1 of the '813 patent is also enabled by the '513application. It is not correct that the only difference between the two claims is one of scope and that the '513 claim is broader. For example, the '513 claim requires use of an isologous region and the '813 claim does not.

In any event, other than meeting the requirement now in claim 1 that the modular PKS from which the first extender unit is excised is different from that from which the second is obtained, the '813 claim does not meet the limitations of present claim 1 that the entire process be carried out by the use of restriction enzymes or that it be confined to excision and replacement of a region "consisting essentially of" a nucleotide sequence encoding the AT domain.

Clearly, there is no anticipation of claim 7 or its dependent claims.

Conclusion

Because the claims are directed to methods generically applicable to modular PKS gene clusters, and in view of the fact that the basic structure of such gene clusters was known at the time the application was made to be substantially similar, applicants have met the written description and enablement requirements of the statute.

The present claims are not anticipated by the cited Katz documents for the reasons set forth above. Prominent among them is that the use of restriction enzymes is required throughout the steps of the method, a procedure not disclosed in any Katz document.

Thus, applicants respectfully request that claims 1-5, 7, 10-13 and 31 be passed to issue.

If minor issues remain that could be resolved in a telephone call, a call to the undersigned is requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 300622000508.

Respectfully submitted,

Dated: August 1, 2007

By: Electronic signature: /Kate H. Murashige/

Kate H. Murashige
Registration No.: 29,959
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
Telephone: (858) 720-5112
Facsimile: (858) 720-5125